99. (New) The isolated polynucleotide of claim 40, wherein said nucleic acid encodes (q). --

Remarks

Claims 25-50 and 60-99 are pending in this application. Claims 11, 13, 17-21, 23-24 and 51-59 have been cancelled. Claim 36 has been amended and new claims 60-99 have been added. Claim 41 has been allowed. Applicants expressly assert that these claims were canceled and amended for the sole purpose of facilitating prosecution or to more clearly define the invention claimed by the Applicant, and not in an effort to overcome the 35 U.S.C. §102 rejections based on cited prior art, or in an effort to overcome rejections based on 35 U.S.C. § 112.

The Examiner objected to the specification because of informalitites. Applicants have amended the specification to more clearly define the relevance of the table on pages 115-119, as was described in the specification, as originally filed, on page 22, second full paragraph, through the top of page 23.

In addition, Applicants have deleted a typographical error from the specification. As would be clear to one of ordinary skill in the art, and as further described below, a frame shift is obviously apparent in the cDNA sequence generated from clone HTAEK53 disclosed in the provisional application U.S. Application No. 60/078,563. The range of nucleotides where the frame shift occurs was misidentified in the instant specification, and has been deleted.

No new matter has been added by way of amendments to the specification or the claims.

Priority:

The Examiner alleges that "no basis for priority is found in US 60/078,563 for SEQ ID NO:1 and 2 nor for ATCC deposit number 209691."

Applicants respectfully disagree and traverse.

The Cytokine Receptor Common Gamma Chain Light (CRCGCL) sequences shown in SEQ ID NO:26 and 27 of the instant application correspond to the Gene 1 sequences shown in SEQ ID NO:11 and 21 of U.S. Provisional Application 60/078,563, filed March 19, 1998, respectively. Table 1 of 60/078,563, a copy of which is provided as Exhibit A,

describes the ATCC deposit number, 209641, and clone ID, HTAEK53, of the cDNA clone containing Gene 1. Clone HTAEK53 is the same as the clone recited in the present application (see, e.g., page 7, lines 3-9). In addition, at page 7, first full paragraph, of the instant application, Applicants disclose, as amended:

> Initially, the sequence of clone HTAEK53 was identified as SEQ ID NO:26 and the deduced amino acid sequence was predicted as SEQ ID NO:27, with a recognition that an apparent frame shift in the sequence existed. This frame shift was easily resolved using standard molecular biology techniques, generating the nucleotide sequence of SEQ ID NO:1 and the deduced amino acid sequence shown as SEQ ID NO:2.

Attached as Exhibit B is an alignment of SEQ ID NO:1 and 26 from the instant application (PF466 SEQ 1 and PF466 SEQ 26, respectively), SEQ ID NO:1 from U.S. Provisional Application 60/086,505 (PF466PP SEQ 1), and SEQ ID NO:11 from U.S. Provisional Application 60/078,563 (PS079A SEQ 11). As one of skill in the art can appreciate, the sequences are identical except for minor sequencing errors such as misidentifed nucleotides, or insertions or deletions of nucleotides in the generated DNA sequence, some of which cause frame shifts in the reading frame of the predicted amino acid sequence (see, e.g., page 9, third full paragraph, of the instant specification). Applicants wish to point out that these sequences were all generated from the same clone, HTAEK53, and thus, except for minor sequencing errors are identical.

Thus, Applicants submit that the basis for priority of SEQ ID NO:1 and 2 and ATCC Deposit Number 209641 is found in U.S. Provisional Application 60/078,563, filed March 19, 1998.

I. Rejections under 35 U.S.C. §112, second paragraph

The Examiner rejects claims 37-40 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinate.

The Examiner contends "[i]t is unclear whether applicant intends the term 'm-371' to designate a range, i.e., from integer m **to** 371, or if the applicant intends the term to designate an arithmetic expression, i.e., interger m **minus** 371."

Applicants thank the Examiner for the opportunity to clarify the use of the term "m-371" to designate a range of amino acid residues.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

II. Rejections under 35 U.S.C. §112, first paragraph

A. The Examiner rejected claims 25-34, 37-40 and 42-50 under U.S.C. § 112, first paragraph, for lack of enablement.

More particularly, the Examiner alleges:

> [T]he specification, while being enabling for nucleic acids that hybridize to the endogenous nucleic acid encoding a polypeptide of SEQ ID NO:2 under stringent conditions (stringent conditions as defined on page 4, lines 23-30), does not reasonably provide enablement for nucleic acids that do not hybridize under the above conditions nor for nucleic acids contained in ATCC Deposit NOS: 209641 and 209641 [sic].

Applicants respectfully disagree and traverse.

Preliminarily, Applicants point out that in order to enable the claimed invention as required by 35 U.S.C. § 112, first paragraph, the specification need only enable a person of skill in the art to make the claimed polynucleotides and practice a single use of the claimed polynucleotides without undue experimentation.[1] Thus, Applicants submit that to be fully enabled, the claimed polynucleotides need merely have application in a single use, such as, for example, as a sex chromosome marker (as disclosed at page 40-41 of the specification) or as a tissue specific marker (as disclosed at page 7, lines 15-24 and page 8, lines 21-33), or to encode a polypeptide that generates an antibody to a protein of the invention which can then be used as a tissue specific marker (as disclosed at page 25, lines 12-20). Applicants submit that, in the present case, since the methods disclosed or otherwise known to skilled artisans at the time of filing could be used, without undue experimentation, for example, to map the claimed polynucleotides to chromosomes, to identify specific tissues, or to generate an antibody that would bind a polypeptide of the invention, the enablement requirement is fully satisfied. For example, polynucleotides encoding polypeptide fragments of at least 30 contiguous amino acids in length, would be useful in routinely generating antibodies against CRCGCL polypeptides (see, e.g., page 18, lines 1-2, pages 27-32, and page 81-82). The

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[1] The Applicant need show utility for only one disclosed purpose. See *Raytheon Co. v. Roper Corp.*, 724 F. 2d 951, 220 U.S.P.Q. 592 (Fed. Cir. 1983, *cert. denied*, 469 U.S. 835 (1984); *Ex parte Lanham*, 121 U.S.P.Q. 223 (Pat. Off. Bd. App. 1958).

polypeptides encoded by the claimed polynucleotide would be particularly useful, for example, in epitope-mapping, in routinely generating CRCGCL specific antibodies which could be used as immunological probes for differential identification of tissues(s) or cell type(s) (see, e.g., page 8, lines 21-26), or in immunoassay techniques, routine in the art, to detect the polypeptides of the present invention. It is noted that it was well known in the art on the priority date of the present application that antibodies can be made to polypeptide fragments even though they may not be immunogenic in an animal using methods such as phage display (as disclosed at page 29, first full paragraph).

With respect to the Examiner's allegation that the specification "does not reasonably provide enablement for nucleic acids that do *not* hybridize . . ." (emphasis added), Applicants submit that the proper inquiry is not whether the specification teaches how to make and use all of the polynucleotides encompassed by the claims, but rather, whether polynucleotides encompassed by the claims have at least a single use, and this use can be confirmed, without undue experimentation, by following procedures either described in the specification or otherwise known in the art. See *In re Angstadt*, 537 F. 2d 498, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976):

> To require such a complete disclosure would apparently necessitate a patent with "thousands of examples . . . More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments . . .

Further, as Judge Rich explained in *In re Vaeck*, 947 F. 2d 488, 20 U.S.P.Q.2d 1438, 1445 (Fed.Cir. 1991), the statutory enablement requirement is satisfied if the specification "adequately guides the worker to *determine,* without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility" (emphasis provided). Since, as discussed above, the disclosed or otherwise known methods of making and screening polynucleotides (including variants and fragments) and polypeptides encoded thereby may be used to make and then determine, without undue experimentation, whether a given polynucleotide encompassed by the claims is able to function as a chromosome marker, a tissue specific marker or to encode a polypeptide that generates antibodies against the polypeptides of the invention, which can then be used as a tissue specific marker, and therefore possesses a disclosed utility, the enablement requirement is fully satisfied. *In re Wands*, 858 F. 2d 731, 8 U.S.P.Q. 2d at 1404; *Ex parte Mark*, 12 U.S.P.Q. 2d 1904, 1906-1907 (B.P.A.I. 1989).

The Examiner further contends:

> Claims 25-36 recite nucleic acids contained in ATCC Deposit NOS:209641 and 209641 [sic]. The instant specification puts forth that 'a representative clone containing *all or most* of the sequence of SEQ ID NO:1 was deposited with the American Type Culture Collection on March 23, 1998, and was given the ATCC Deposit Number 209691. A second clone was deposited with the ATCC on February 25, 1998, and given ATCC Deposit Number 209641'... The specification has failed to provide enabling basis for the claimed invention...

In addition, the Examiner alleges:

> If *most* of the sequence of SEQ ID NO:1, but not *all* of the sequence, is contained in ATCC Deposit Number 209691, then in order to use the claimed invention, one of skill in the art would need to know which sequences of SEQ ID NO:1 were present in ATCC Deposit Number 209691 and which sequences were not present.

The Examiner further contends:

> The instant application has failed to provide guidance to as to the nature, function, or identity of ATCC Deposit Number 20964 [sic], nor of the relationship, if any, between SEQ ID NO:1 and ATCC Deposit Number 20964 [sic]. One of skill in the art would, therefore, be unable to use the claimed invention.

Applicants respectfully disagree and traverse. U.S. Provisional Application Serial No. 60/078,563, filed March 19, 1998, discloses the sequence of the cDNA contained in cDNA Clone ID HTAEK53 (SEQ ID NO:11 and 21), which was deposited on February 25, 1998 and given the ATCC Deposit Number 209641. As mentioned previously, the sequence initially determined for this clone contained sequencing errors which resulted in a frame shift in the predicted amino acid sequence. These sequences are provided in SEQ ID NO:26 and 27 of the instant application. An alignment of SEQ ID NO:11 of 60/078,563, SEQ ID NO:1 of 60/086,505, and SEQ ID NO:26 and SEQ ID NO:1 of the instant application is provided as Exhibit B.

A second U.S. Provisional Application Serial No. 60/086,505, filed May 22, 1998, discloses the corrected sequence of clone HTAEK53 (SEQ ID NO:1 and 2), which was deposited a second time on March 13, 1998. These sequences are provided as SEQ ID NO:1 and 2 of the instant specification. Thus, using the disclosure of U.S. Provisional Applications 60/086,505 and 60/078,563, and the instant application, one of skill in the art could have

easily determined that the same cDNA clone, uniquely described as HTAEK53, was deposited as both ATCC Deposit Number 209641 and 209691.

Applicants wish to draw the Examiner's attention to the second full paragraph on page 7 of the instant application, wherein Applicants describe the sequence contained in the deposit as, "having a total of 1573 nucleotides, which encodes a predicted open reading frame of 371 amino acid residues. (See Figures 1A-1B.)" In addition, in both Table 1 of U.S. Provisional Application 60/078,563 and at page 68, first full paragraph of the instant application, Applicants disclose that the cDNA in the deposited clone, uniquely identified as HTAEK53, is inserted into a Uni-ZAP XR vector.

Thus, the instant application as originally filed discloses the nature, function and identity of ATCC Deposit Number 209641.

The Examiner further contends:

> [T]he specification has not provided guidance as to which nucleic acids encoding the almost infinite number amino acid substitutions recited in claims 25 and 34 nor which nucleic acids encoding a polypeptide of SEQ ID NO:2 but which differ from SEQ ID NO:1 due to the redundancy of the genetic code would be useful as a tissue specific probe.

As discussed at length above, in order to enable the claimed invention as required by 35 U.S.C. § 112, first paragraph, the specification need only enable a person of skill in the art to make the claimed polynucleotides and practice a single use of the claimed polynucleotides without undue experimentation. Applicants submit that, in the present case, the claimed polynucleotides which encode a polypeptide of SEQ ID NO:2 but which differ from SEQ ID NO:1 due to the redundancy of the genetic code would be particularly useful, for example, in epitope-mapping, in routinely generating CRCGCL specific antibodies which could be used as immunological probes for differential identification of tissues(s) or cell type(s) (see, e.g., page 8, lines 21-26), or in immunoassay techniques, routine in the art, to detect the polypeptides of the present invention. As previously mentioned, polynucleotides encoding polypeptide fragments of at least 30 contiguous amino acids in length, would be useful in routinely generating antibodies against CRCGCL polypeptides (see, e.g., page 18, lines 1-2, pages 27-32, and page 81-82). It is again noted that it was well known in the art on the priority date of the present application that antibodies can be made to polypeptide fragments even though they may not be immunogenic in an animal using methods such as phage display (as disclosed at page 29, first full paragraph).

The specification teaches which amino acid residues comprise epitope-bearing portions of CRCGCL (see, e.g., page 24, lines 14-16). With this information, one of ordinary skill in the art would know which amino acid residues of the polypeptide could be substituted and still constitute a polypeptide which is capable of raising antibodies to CRCGCL. For example, amino acids +1 to +371, as recited in claim 25(c), comprise an epitope bearing portion at amino acids +286 to +293. If up to 18 amino acids (5% of the total amino acids present between +1 and +371) were to be substituted within the sequence of amino acids between +1 and +371, one of ordinary skill in the art would know not to substitute amino acids +286 to +293 in order to produce a polypeptide which is still useful for raising antibodies to this epitopic region of CRCGCL. Thus, the above shows that one of ordinary skill in the art could routinely determine which amino acids could be substituted without further changing the utility of the polypeptide as related to raising antibodies which could be used, for example, as immunological probes for differential identification of tissues(s) or cell type(s).

Further, Applicants direct the Examiner's attention to pages 15 to 16 of the specification which discloses Bowie, J.U. *et al., Science 247:*1306-1310 (1990) (see, e.g., page 15, lines 20-21). Applicants submit that this reference is adequate in giving one skilled in the art guidance concerning which amino acid changes are phenotypically silent. In addition, the specification discloses Cunningham and Wells, *Science 244:*1081-1085 (1989) which teaches how to determine which amino acids of a protein are essential to its function (see, e.g., page 15, line 34). Applicants believe that these disclosures are sufficient to enable one skilled in the art to make amino acid substitutions, deletions, and insertions up to 5% of the total number of amino acids provided without changing the function of the polypeptide.

In view of the above discussion, Applicants believe the Examiner's concerns have been fully addressed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 25-34, 37-40 and 42-45 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

B. In addition, the Examiner rejects claims 51-59 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

More particularly, the Examiner alleges:

> [D]ue to the large quantity of experimentation necessary to determine which cell types, if any could be used with the claimed invention and then to determine the nature of the regulation of the cells that are to be used, the absence of

> working examples wherein CRCGCL is used to regulate cell proliferation and/or differentiation, the complex nature of the art..., undue experimentation would be required of the skilled artisan to use the claimed invention, if in fact if can be used as claimed.

Applicants respectfully disagree and traverse.

Applicants submit that, in the instant case, since the disclosed or otherwise known methods of making and screening polypeptides may be used to determine, without undue experimentation, whether a given CRCGCL polypeptide encoded by a polynucleotide encompassed by the claims regulates the differentiation and/or proliferation of cells, the enablement requirement is fully satisfied. *In re Wands*, 858 F.2d at 738, 8 U.S.P.Q.2d at 1404; *Ex parte Mark*, 12 U.S.P.Q.2d 1904, 1906-1907 (B.P.A.I. 1989).

The Examiner further rejects claims 51-59 for lack of enablement because the claims "recite ATCC Deposit NOS: 209641 and 209641 [sic]." Applicants have fully addressed this issue in the above discussion.

Nonetheless, solely in the interest of expediting prosecution, Applicants have canceled claims 51-59. Accordingly, the basis of this rejection has been overcome or obviated and the rejection should be withdrawn.

III. Rejections Under 35 U.S.C. § 102

The Examiner rejected claims 36-38 under 35 U.S.C. § 102(b) as allegedly being anticipated by GenEmbl accession number X91553.

More specifically, the Examiner contends:

> Claims 36-38 claim a nucleic acid that hybridizes to a polynucleotide of SEQ ID NO:1 (claim 36) or encoding a polypeptide comprising at least one amino acid residue of SEQ ID NO:2 (claims 37c and 38). GenEmbl accession number X91553 discloses a polynucleotide that is 100% identical to SEQ ID NO:1 over the range of positions 778-806, and would therefore hybridize to SEQ ID NO:1 under highly stringent conditions and would also be expected to encode a polypeptide having a sequence identical to positions 256-264 of SEQ ID NO:2.

Applicants respectfully disagree with the rejection over GenEmbl accession number X91553. However, in the interest of facilitating prosecution, Applicants have amended claim

36 to recite "wherein said polynucleotide is not Genbank Accession No. X91553." Support for this language can be found in the instant specification at page 23, lines 11-14.

Accordingly, Applicants believe the Examiner's concerns have been fully addressed and respectfully request reconsideration and withdrawal of the rejection of claims 36-38 under 35 U.S.C. § 102(b).

Conclusion

In view of the foregoing remarks, applicants believe that this application is now in condition for allowance.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated June 2, 2000

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